

**REMARKS**

Claims 7-29, 33-37, 43, 55, 56, 59-63, 67, 71-79, 81-87, 92-95, 117, 118, and 120-129 are currently pending. Among them, Claims 24-29, 82-87, 117, 118, 124, and 125 are allowed.

Applicants thank the Examiner for withdrawing the finality of the Office Action issued on February 14, 2005.

Applicants also submit herewith a supplemental IDS, and respectfully request the Examiner to consider the references cited therein.

Applicants respectfully request reconsideration in view of the following remarks and claim amendments. Issues raised in the Office Action will be addressed below in the order they appear in the Action.

**Objection to the Specification**

The Office Action objects to the specification for alleged non-compliance with the Sequence Rules and the incorporation of new matter.

Applicants have previously filed a **first** sequence listing on July 18, 2002; then a **second** sequence listing on August 1, 2003, which replaces the July 18, 2002 sequence listing; and finally a **third** sequence listing on January 28, 2004, which replaces the August 1, 2003 sequence listing. Applicants submit that the **third, January 28, 2004** is the sequence listing **currently on file**. Therefore, Applicants refer to the SEQ ID NOs in the Jan. 28, 2004 sequence listing in the arguments and amendments below.

To facilitate an easy comparison between the July 18, 2002 sequence listing (which SEQ ID NOs the Examiner is apparently using) and the Jan. 28, 2004 sequence listing, Applicants have summarized the differences between these two sequence listings.

July 18, 2002 sequence listing ( <b>first</b> )	January 28, 2004 sequence listing (third / <b>current</b> )
SEQ ID NOs: 1-27	SEQ ID NOs: 1-27 (Same)
<b>SEQ ID NO: 28</b> (was redundant with SEQ ID NO: 16 above)	*Replaced the redundant SEQ ID NO: 28 with the GPC-8-1 VL sequence
SEQ ID NOs: 29 & 30	SEQ ID NOs: 29 & 30 (Same)
<b>SEQ ID NO: 31</b> (was redundant with	*Replaced the redundant SEQ ID NO: 31 with the

SEQ ID NO: 17 above)	GPC-8-9 VL sequence
<b>SEQ ID NO: 32</b> (was redundant with SEQ ID NO: 18 above)	*Replaced the redundant SEQ ID NO: 32 with the GPC-8-18 VL sequence
SEQ ID NOs. 33-44	SEQ ID NOs: 33-44 (Same)
<b>SEQ ID NO: 45</b> (was redundant with SEQ ID NO: 41 above)	*Replaced the redundant SEQ ID NO: 45 with the GPC-8-6-2 VL sequence
SEQ ID NO: 46	SEQ ID NO: 46 (Same)
<b>SEQ ID NO: 47</b> (was redundant with SEQ ID NO: 41 above)	*Replaced the redundant SEQ ID NO: 47 with the GPC-8-6-19 VL sequence
SEQ ID NO: 48	SEQ ID NO: 48 (Same)
<b>SEQ ID NO: 49</b> (was redundant with SEQ ID NO: 41 above)	*Replaced the redundant SEQ ID NO: 49 with the GPC-8-6-27 VL sequence
SEQ ID NO: 50	SEQ ID NO: 50 (Same)
<b>SEQ ID NO: 51</b> (was redundant with SEQ ID NO: 41 above)	*Replaced the redundant SEQ ID NO: 51 with the GPC-8-6-45 VL sequence
SEQ ID NO: 52	SEQ ID NO: 52 (Same)
<b>SEQ ID NO: 53</b> (was redundant with SEQ ID NO: 41 above)	*Replaced the redundant SEQ ID NO: 53 with the GPC-8-6-47 VL sequence
SEQ ID NO: 54	SEQ ID NO: 54 (Same)
<b>SEQ ID NO: 55</b> (was redundant with SEQ ID NO: 41 above)	*Replaced the redundant SEQ ID NO: 55 with the GPC-8-27-7 VL sequence
SEQ ID NO: 56	SEQ ID NO: 56 (Same)
<b>SEQ ID NO: 57</b> (was redundant with SEQ ID NO: 41 above)	*Replaced the redundant SEQ ID NO: 57 with the GPC-8-27-10 VL sequence
SEQ ID NO: 58	SEQ ID NO: 58 (Same)
<b>SEQ ID NO: 59</b> (was redundant with SEQ ID NO: 22 above)	Replaced the redundant SEQ ID NO: 59 with the former SEQ ID NO: 63
SEQ ID NOs: 60-62	SEQ ID NOs: 60-62 (Same)
<b>SEQ ID NO: 63</b>	Moved to SEQ IS NO: 59 (see above)

\* see the paragraph bridging pages 46 and 47 of Applicants' response filed on January 26, 2004, which refers to a January 5, 2004 interview with the Examiner, and the Examiner's concurrence with this approach.

Based on the January 28, 2004 sequence listing, Applicants have amended the specification to add proper SEQ ID NOs to the polynucleotide and polypeptide sequences pursuant to 37 C.F.R. §§ 1.821-1.825. Applicants submit that no new matter is introduced by the submission of the instant sequence listing.

Regarding the specific issues raised in the Office Action, Applicants submit that the Office Action appears to have confused certain CDR region sequences with VH or VL domain sequences. For example, the Office Action refers to "VH domain of GPC-1" as "residues 100-109 of SEQ ID NO: 37." However, the VH domain of GPC-1 is a 120-amino acid polypeptide disclosed in Figure 15 and SEQ ID NO: 37. It **includes**, but is **not itself** the peptide sequence "QYGHRGGFDH," which is the "VH-CDR3-Seq" of GPC-1 (see SEQ ID NO: 19 and the first line of the amended Table 1). Although this sequence also appears as "residues 100-109 of SEQ ID NO: 37," it should nevertheless be properly referred to as "SEQ ID NO: 19."

Thus, when the Office Action points out, on the top of page 3 of the Office Action, that "GPC-8-1 ... is QSYDFSHY," the Office Action is in fact referring to the **VL-CDR3-Seq** of GPC-8-1, which cannot be found in the current SEQ ID NO: 48, because SEQ ID NO: 48 represents the 109-amino acid VL sequence of GPC-8-10 (not GPC-8-1). Instead, support for QSYDFSHY can be found in Table 1, and this sequence is properly referred-to as "SEQ ID NO: 24." See amended Table 1. In addition, GPC-8-1 VL is the new SEQ ID NO: 28 in the January 28, 2004 (current) sequence listing, see the comparison table above, and the associated footnote.

Similarly, the peptide sequence QSYDIQLH is not GPC-8-9, but rather the **VL-CDR3-Seq** of GPC-8-9 (SEQ ID NO: 25 in the January 28, 2004 (current) sequence listing). The Examiner points out that the QSYDIQLH sequence is not SEQ ID NO: 31 in the July 18, 2002 sequence listing. This is correct, but this is because Applicants are referring to the SEQ ID NO in the January 28, 2004 (current) sequence listing. The former SEQ ID NO: 31 in the July 18, 2002 sequence listing is redundant with SEQ ID NO: 17, and is thus replaced by the GPC-8-9 VL sequence in the January 28, 2004 (current) sequence listing (see the comparison table above).

Similarly, QSYDFSIY is not GPC-8-18, but the **VL-CDR3-Seq** of GPC-8-18 (see SEQ ID NO: 27 and amended Table 1). GPC-8-18 VL is the new SEQ ID NO: 32 in the January 28, 2004 (current) sequence listing, replacing the redundant former SEQ ID NO: 32 (see the comparison table above).

The Office Action also objected to the specification for allegedly incorporating new matter, because “the disclosure of the CDR regions of the isolated clones on Table 1, does not provide adequate support for the entire sequence comprising the clone.” Applicants respectfully disagree.

First of all, Table 1 and all sequences listed therein are present in the original specification as filed. Even assuming, for the sake of argument, that there is no nexus between the disclosed CDR sequences and the remaining framework region sequences, as the Office Action alleges, Applicants cannot introduce new matter simply by inserting certain SEQ ID NOs.

Secondly, as argued below, the instant specification provides not only the detailed framework sequences, but also numerous representative MS-GPC VH and VL sequences (see Figure 15) that include the CDR regions as well as the surrounding framework sequences. Thus, contrary to what the Office Action alleges, Applicants do provide “the entire sequence comprising the clone.”

The Office Action also objects to the sequence listing filed on August 1, 2003 as containing new matter, and as being substantially different from the one filed on July 18, 2002.

Applicants submit that the January 28, 2004 sequence listing is the current sequence listing on file. The August 1, 2003 sequence listing is replaced by the January 28, 2004 sequence listing. Thus regardless of the merits of this objection, the objection is rendered moot.

However, in order to facilitate the understanding of the correlation between the disclosed sequences and their SEQ ID NOs in the current sequence listing, Applicants submit that in Claim 22, the GPC-1 clone relates to SEQ ID NOs: 37 and 38, which are the full-length VH and VL sequences, respectively.

SEQ ID NO: 19 as disclosed in Table 1 is the CDR3 region sequence of the GPC-1 VH chain. SEQ ID NO: 19 corresponds to residues 100-109 of SEQ ID NO: 37.

SEQ ID NO: 12 as disclosed in Table 1 is the CDR1 region sequence of the GPC-1 VL chain. SEQ ID NO: 12 corresponds to residues 23-35 of SEQ ID NO: 38.

SEQ ID NO: 59 (former SEQ ID NO: 63 in the July 18, 2002 sequence listing) as disclosed in Table 1 is the CDR3 region sequence of the GPC-1 VL chain. SEQ ID NO: 59 corresponds to residues 90-97 of SEQ ID NO: 38.

Reconsideration and withdrawal of the specification objections are respectfully requested.

*Claim rejections under 35 U.S.C. § 112, first paragraph – written description*

Claims 7-23, 33-37, 43, 55, 56, 59-63, 67, 71-79, 81, 92-95, 120-123, and 126-129 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the Office Action alleges that these claims are drawn to compositions comprising full length sequences of the variable chains of certain disclosed VH/VL domain sequences (such as SEQ ID NO: 37), but the specification fails to provide support for a multivalent polypeptide comprising the entirety of SEQ ID NOs: 37-58, because “disclosure of a CDR sequence in the originally filed specification does not adequately describe an antibody based variable chain sequence, because said variable chain comprises framework region sequences which are extraneous to the CDR sequence and which have no direct nexus to the sequence of the CDR regions.” Thus, the Office Action asserts that a skilled artisan “would reasonably conclude that applicant was not in possession of the entirety of the claimed variable chain sequences at the time the application was filed.” Applicants respectfully disagree.

As explained above, Applicants have fully described the **full-length sequence** of the eleven (11) VH and VL domains in Figure 15 as-filed (see SEQ ID NOs: 37-44, 46, 48, 50, 52, 54, 56, and 58). These sequences not only contain the CDR regions, but also the framework regions showing the context in which these CDR regions appear.

In addition, Applicants have also described in Table 1 and 2 numerous CDR region sequences for derivative VH and VL sequences. Although these derivative VH and VL sequences are not explicitly shown in the original Figure 15, a skilled artisan could immediately envision the full-length sequences of these derivative VH and VL sequences (and scFv, Fab, and IgG sequences, etc. that encompass such VH and VL sequences). This is because the derivative VH and VL sequences are identical to the original VH and VL sequences from which they



derive, except in the indicated CDR regions (see the random optimization experiments described in detail in Example 4). For example, GPC-8-1 derives from GPC-8. Thus the VH sequences for GPC-8-1 and GPC-8 are identical (see Table 1). The only difference between these two, according to Table 1, appears to be in the VL CDR3 region (compare SEQ ID NO: 22 with SEQ ID NO: 24).

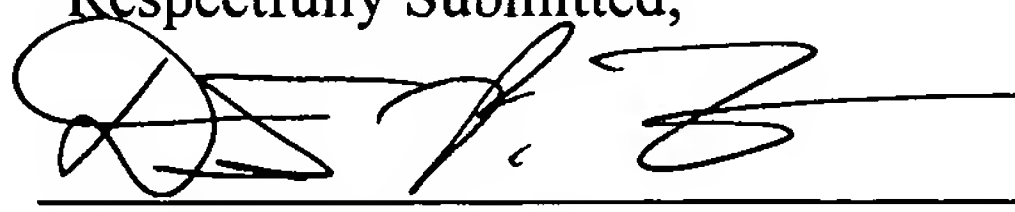
Applicants wish to bring the Examiner's attention to the paragraph bridging pages 46 and 47 of the response filed on January 26, 2004. There, Applicants indicated that, during a January 5, 2004 interview, the Examiner concurred with Applicants' explanation relating to the sequence disclosure of the derivative clones whose full-length sequences are not explicitly listed in Figure 15 as filed, but whose CDR region sequences are unambiguously identified in Table 1. Therefore, all claimed GPC clone sequences are fully described in the instant specification, and no new matter is introduced either by the current sequence listing, or by the specification. Reconsideration and withdrawal of the written description rejection under 35 U.S.C. § 112, first paragraph are respectfully requested.

### **CONCLUSION**

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Applicants authorize any extension fee (if necessary) and any other fee required for timely consideration of this submission to be charged to **Deposit Account No. 18-1945**, Order No. **GPCG-P01-003**.

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Respectfully Submitted,  
  
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